

REMARKS

Applicants respectfully request entry of the amendment and reconsideration of the claims. Claim 88 has been amended to further clarify the invention as claimed. Claims 31-50 and 92 have been cancelled without prejudice or disclaimer. Claims 93-111 are newly presented and correspond to cancelled claims 31 and 33-50 respectively. After entry of the amendment, claims 88-91 and 93-111 will be pending.

The amendment is supported throughout the specification, including for example at page 7, lines 14-17, page 12, lines 14-16, page 16, line 12 to page 17, line 29, page 33, lines 4-17, and Examples 5, 6A, and 6B. Applicants submit the amendment does not introduce any new matter.

Specification

The Office Action objected to the title as not being properly descriptive of the claims. Applicants have amended the title as required by the Examiner. Applicants submit the new title complies with the requirements of MPEP § 606.01. Withdrawal of the objection is respectfully requested.

Claim Objections

The Office Action objected to the ordering of the claims because the independent claims are not the first claims presented. Claims 31-50 have been cancelled solely for the purpose of presenting the independent claims first as required by the Examiner. New claims 93-111 correspond to cancelled claims 31 and 33-50 respectively.

Claims 40, 42, 46, and 88 were objected to as containing one or more informalities. Applicants have amended the claims as required by the Examiner. Withdrawal of the claim objections is respectfully requested.

Indefinite

Claims 36, 28, 41, 42, and 90 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Applicants respectfully traverse this rejection.

The Office Action alleges that the term “about” as used in the claims to describe the wavelength of light is indefinite. Applicants respectfully do not agree.

The test for definiteness under 35 U.S.C. § 112, second paragraph, is whether “those skilled in the art would understand what is claimed when the claim is read in light of the specification.” *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576 (Fed. Cir. 1986). Furthermore, a claim term that is not used or defined in the specification is not indefinite if the meaning of the claim term is discernible. *Bancorp Services, L.L.C. v. Hartford Life Ins. Co.*, 359 F.3d 1367, 1372 (Fed Cir. 2004). One of skill in the art would recognize that the ability to accurately measure or identify a specific wavelength of light is dependent upon the sensitivity of the instrumentation employed to measure or identify said wavelength and would understand that the term “about” as used in the context of the claims and specification means the wavelength plus or minus the standard error associated with such instrumentation.

The Office Action alleges the phrase “the plane of the disulfide bridge” in claim 41 is unclear. For purposes of clarity, Applicants have amended claim 41 to recite “the plane of the absorbing dipole of the disulfide bridge”.

The Office Action alleges the terms “over-represented” and “under-represented” recited in claim 42 are unclear. Applicants have amended the claims to further clarify the invention as claimed. Claim 42 as amended recites the frequency of occurrence of certain amino acid residues in the irradiated peptide or protein relative to the frequency of occurrence of said amino acid residues in proteins in general.

In view of the forgoing, Applicants submit the claims comply with § 112, second paragraph. Withdrawal of the rejection is respectfully requested.

Written Description

Claims 31-50 and 88-92 were rejected under 35 U.S.C. § 112, first paragraph as lacking written description. Applicants respectfully traverse this rejection.

The written description requirement must be applied in the context of the particular invention and state of the knowledge. *Capon v. Eschar*, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005). It is unnecessary to spell out every detail of the invention in the specification. Only enough must be included to convince a person of skill in the art that the inventor possessed the

invention. *Falkner v. Inglis*, No. 05-1234, slip. op. at 14 (Fed Cir. May 26, 2006) (citing *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 F.3d 1336, 1345 Fed. Cir. 2005). An actual reduction to practice is not required for written description. *Falkner v. Inglis*, No. 05-1324, slip. op. at 13 (Fed. Cir. May 26, 2006). Applying these standards, Applicants submit the specification sufficiently describes the claims as amended.

The Office Action alleges the specification does not adequately support irradiating any protein or peptide at any wavelength to create a thiol group. Applicants respectfully do not agree. However, without acquiescing to the rejection and solely for the purpose of advancing prosecution, claim 88 has been amended to clarify that (1) the protein or peptide comprises one or more aromatic amino acid residue within 10 angstrom (\AA) of a disulfide bridge and (2) the protein or peptide is irradiated with light of a wavelength that excites said one or more aromatic amino acid residues to create a thiol group in the protein or peptide by disulfide bridge disruption.

The specification discloses that disulfide bridges located in close proximity to aromatic amino acids are the most vulnerable to UV-induced disruption and that the presence of a disulfide bridge with an aromatic residue such as Trp as a close spatial neighbor in a protein occurs frequently in nature, indicating that photo-induced disulfide bridge disruption is a widespread phenomenon (see specification, for example, at page 14, lines 3-17). The specification discloses guidelines for identifying which disulfide bridges in a protein are capable of light-induced coupling (see the specification, for example, at page 16, line 23 to page 17, lin3 29). The specification discloses guidelines for irradiating the aromatic amino acids in close spatial proximity to a disulfide bridge, including absorption maxima, ranges of wavelengths and specific wavelengths for exciting specific aromatic residues or combinations of aromatic residues (see specification, for example, at page 15, line 12 to page 16, line 10). The specification also provides multiple examples of proteins from different species, families and classes (e.g., cutinase, hen egg white lysozyme, *Rhizopus niveus* triglyceride lipase, human plasminogen, human placental alkaline phosphatase, chymosin B, and immunoglobulin IgG) shown to comprise light-inducible disulfide bridges according to the guidelines provided in the specification (see the specification, for example, at Example 4 and Figs. 8A-F). Utilizing cutinase, lysozyme,

and chymosin as exemplary proteins, the working examples show that the identified light-inducible disulfide bridges form free SH groups upon irradiation and that the created reactive thiol group can be coupled to a carrier comprising a thiol-binding ligand (see, specification, for example at Examples 5, 6A, and 6B).

In view of the foregoing, Applicants submit the specification provides sufficient detailed, relevant identifying characteristics such that that one skilled in the art can reasonably conclude that Applicants had possession of the invention as claimed.

The Office Action alleges “coupling” as recited in the claims includes any kind of association or immobilization. Applicants respectfully do not agree. However, without acquiescing to the rejection and solely for the purpose of advancing prosecution, claim 88 has been amended to clarify that that protein or peptide is coupled to a carrier comprising Au or a thiol binding ligand through the created thiol group. As discussed above, the protein or peptide is irradiated with light of a wavelength that excites the one or more aromatic amino acid residues to create a thiol group in the protein or peptide by disulfide bridge disruption.

For at least these reasons, Applicants respectfully submit the specification fully describes the claims as amended. Withdrawal of the written description rejection is respectfully requested.

Enablement

Claims 31-50 and 88-92 were rejected under 35 U.S.C. § 112, first paragraph as lacking enablement. Applicants respectfully traverse this rejection.

The Office Action alleges the specification does not enable irradiating any protein or peptide at any wavelength to create a thiol group without undue experimentation. Applicants respectfully do not agree. However, without acquiescing to the rejection and solely for the purpose of advancing prosecution, claim 88 has been amended to clarify that (1) the protein or peptide comprises one or more aromatic amino acid residue within 10 angstrom (\AA) of a disulfide bridge and (2) the protein or peptide is irradiated with light of a wavelength that excites said one or more aromatic amino acid residues to create a thiol group in the protein or peptide by disulfide bridge disruption.

An enabling disclosure requires a reasonable correlation to the scope of the claims. As long as the specification discloses at least one method for making and using the claimed

invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied (*In re Fischer*, 427 F.2d 833, 839 (CCPA 1970)). For a claimed genus, representative examples coupled with a statement applicable to the genus as a whole are ordinary sufficient to comply with the enablement requirement (MPEP § 2164.02). The disclosure of a test with every species covered by a claim is not necessary for establishing enablement under 35 U.S.C. § 112, first paragraph. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1998). A substantial amount of experimentation is permissible if the experimentation is routine or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) (emphasis added); see also *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976).

Applying these standards, Applicants submit the claims as amended could be practiced without undue experimentation. The specification provides guidance and working examples for identifying proteins and polypeptides comprising one or more aromatic amino acid residue within 10 angstrom (Å) of a disulfide bridge, irradiating said proteins and polypeptides to create a reactive thiol group, and coupling said irradiated proteins and polypeptides to a carrier comprising a thiol-binding ligand.

As discussed above, the specification discloses that disulfide bridges located in close proximity to aromatic amino acids are the most vulnerable to UV-induced disruption and that the presence of a disulfide bridge with an aromatic residue such as Trp as a close spatial neighbor in a protein occurs frequently in nature, indicating that photo-induced disulfide bridge disruption is a widespread phenomenon. The specification discloses guidelines for identifying which disulfide bridges in a protein are capable of light-induced coupling and guidelines for irradiating the aromatic amino acids in close spatial proximity to a disulfide bridge, including absorption maxima, ranges of wavelengths and specific wavelengths for exciting specific aromatic residues or combinations of aromatic residues. Using these guidelines, the specification shows multiple examples of proteins from different species, families and classes (e.g., cutinase, hen egg white lysosyme, *Rhizopus niveus* triglyceride lipase, human plasminogen, human placental alkaline phosphatase, chymosin B, and immunoglobulin IgG) that comprise light-inducible disulfide bridges. The specification shows that the identified light-inducible disulfide bridges in a sample of

proteins (*e.g.*, cutinase, lysozyme, and chymosin) form free SH groups upon irradiation and that the created reactive thiol group can be coupled to a carrier comprising a thiol-binding ligand.

The Office Action alleges “coupling” as recited in the claims includes any kind of association or immobilization and is not enabled by the specification. Applicants respectfully do not agree. However, without acquiescing to the rejection and solely for the purpose of advancing prosecution, claim 88 has been amended to clarify that that protein or peptide is coupled to a carrier comprising Au or a thiol binding ligand through the created thiol group. As discussed above, the specification discloses guidelines for irradiating the protein or peptide with light of a wavelength that excites the one or more aromatic amino acid residues to create a thiol group in the protein or peptide by disulfide bridge disruption and coupling the protein or peptide to a carrier comprising a thiol-binding ligand through the created thiol group.

The Office Action alleges the claims are unpredictable for any coupling any protein or peptide to a carrier because the specification only discloses such coupling with cutinase and the art (Prombers, 1999, FEBS Lett., 456:409-416) only discloses one species (*e.g.*, cutinase) encompassed within the scope of the claims. Applicants respectfully do not agree.

Prombers does not teach or suggest any species within the scope of the claims as amended for the reasons discussed below.

As discussed above, the specification provides guidance and working examples for identifying proteins and polypeptides comprising one or more aromatic amino acid residue within 10 angstrom (Å) of a disulfide bridge, irradiating said proteins and polypeptides to create a reactive thiol group, and coupling said irradiated proteins and polypeptides to a carrier comprising a thiol-binding ligand. The specification shows multiple examples of proteins from different species, families and classes (*e.g.*, cutinase, hen egg white lysozyme, *Rhizopus niveus* triglyceride lipase, human plasminogen, human placental alkaline phosphatase, chymosin B, and immunoglobulin IgG) that comprise light-inducible disulfide bridges. In a sample of these proteins (*e.g.*, cutinase, lysozyme, and chymosin) the specification shows that (1) the identified light-inducible disulfide bridges in these proteins form free SH groups upon irradiation and (2) the created reactive thiol group can be coupled to a carrier comprising a thiol-binding ligand.

In view of the guidance and working examples provided in the specification, one of skill in the art would reasonably expect that irradiating a protein or peptide comprising one or more aromatic amino acid residue within 10 angstrom (\AA) of a disulfide bridge with light of a wavelength that excites said one or more aromatic amino acid residues would create a thiol group in the protein or peptide by disulfide bridge disruption.

In view of the foregoing, Applicants submit the full scope of the claims could be practice without undue experimentation. Accordingly, withdrawal of the enablement is respectfully requested.

Anticipation

Claims 31-49 and 88-92 were rejected under 35 U.S.C. § 102(b) as being anticipated by Prombers, 1999, FEBS Lett., 456:409-416. Applicants respectfully traverse this rejection.

In order to anticipate a claim, the prior art reference must teach each and every element of the claim. *Verdegall Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987); MPEP § 2131. The identical invention must be shown in the same complete detail as is recited by the claims. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989).

Claim 88 as amended recites irradiating the protein or peptide with light of a wavelength that excites the one or more aromatic amino acid residues to create a thiol group in the protein or peptide by disulfide bridge disruption and coupling the protein or peptide to a carrier comprising Au or a thiol-binding ligand through the created thiol group. Prombers does not disclose a carrier comprising Au or a thiol-binding ligand or coupling the protein or peptide to said carrier through the created thiol group. Prombers therefore does not disclose all the elements of the claims.

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300

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Denise M. Kettelberger, Ph.D., J.D.
Reg. No. 33,924
DMK:EED:jrm

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PATENT TRADEMARK OFFICE